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THE POSTWAR HOSPITALIZATION EXPERIENCE OF U.S. VETERANS OF THE PERSIAN GULF WAR

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ABSTRACT

Background Since the Persian Gulf War ended in 1991, many veterans of that conflict have reported diverse, unexplained symptoms. To evaluate the health of Gulf War veterans, we studied their postwar hospitalization experience and compared it with that of other military personnel serving at the same time who did not go to the Persian Gulf.

Methods Using a retrospective cohort approach and data from Department of Defense hospitals, we studied hospitalizations of 547,076 veterans of the Gulf War who were serving in the Army, Navy, Marine Corps, and Air Force and 618,335 other veterans from the same era who did not serve in the Persian Gulf. Using multivariate logistic-regression models, we analyzed risk factors for hospitalization both overall and in 14 broad diagnostic categories during three periods from August 1991 through September 1993 (a total of 45 comparisons).

Results After the war, the overall odds ratio for hospitalization of the Gulf War veterans was not higher than that of the other veterans, even after adjustment for selection effects related to deployment. In 16 of the 42 comparisons involving specific diagnoses, the risk of hospitalization among Gulf War veterans differed significantly from that among other veterans. Among these 16 comparisons, Gulf War veterans were at higher risk in 5: neoplasms (largely benign) during 1991, diseases of the genitourinary system during 1991, diseases of the blood and blood-forming organs (mostly forms of anemia) during 1992, and mental disorders during both 1992 and 1993. The differences were not consistent over time and could be accounted for by deferred care, postwar pregnancies, and postwar stress.

Conclusions During the two years after the Persian Gulf War, there was no excess of unexplained hospitalization among Americans who remained on active duty after serving in that conflict. (N Engl J Med 1996;335:1505-13.)

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DURING the Persian Gulf War, there were far fewer combat and medical casualties among U.S. military personnel than expected.¹⁻⁷ Since returning from the Persian Gulf, however, some veterans have reported a variety of symptoms.⁷⁻⁹ The Departments of Defense, Veterans Affairs, and Health and Human Services have responded with a number of investiga-

tions¹⁰⁻¹⁴ and programs of comprehensive clinical evaluation for Gulf War veterans and their families.^{15,16} Panels of distinguished scientists continue to examine environmental, medical, and laboratory data to determine whether the veterans' symptoms are associated with a common exposure and whether the various combinations of symptoms point to a unique illness.^{11,17,18} Thus far, these evaluations have not implicated specific exposures or a recognized disease process as causing the multiple symptoms, nor have they identified a new illness. Reports of unexplained symptoms have received much attention in the media and have heightened national concern.^{7-9,19-23} Recently, the U.S. government set up a number of telephone hot lines, established a presidential advisory committee, and appropriated more than \$20 million for federal and nonfederal research on the health of Gulf War veterans.²⁴⁻²⁷

Using the computerized hospitalization records of the Department of Defense, we conducted a study to determine whether Gulf War veterans were at increased risk for hospitalization after the war, as compared with veterans from the same era who did not go to the Persian Gulf.

METHODS

Sources of Data

The data on service in the Gulf War, demographic variables, military separations, and hospitalizations that were used in this study were obtained from the Defense Manpower Data Center, Monterey Bay, California. Data on Gulf War service were compiled from Army, Navy (including Marine Corps), and Air Force records of unit-deployment locations and pay for exposure to hostile fire. Demographic data were obtained from routine data files on U.S. military personnel.

Study Population

On January 21, 1991, President George Bush issued an executive order²⁸ designating much of the land mass of the Arabian Peninsula and the seas surrounding it as a combat zone. Military personnel

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deployed to serve in the Gulf War for one or more days between August 8, 1990, and July 31, 1991, were considered Gulf War veterans. A total of 579,931 of the 696,562 U.S. Gulf War veterans (83.3 percent) served on regular, active duty in the Army, Navy (including the Marine Corps), or Air Force. Since such personnel are rarely hospitalized in facilities other than those operated by the Department of Defense and since data on their hospitalizations were readily available from that department, we examined the hospitalization experience of these veterans. The hospitalizations of U.S. reserve and National Guard forces could not be studied with our data.

Using a random-number procedure, the Defense Manpower Data Center selected a comparison group of 700,000 military personnel on active duty who were listed on the Department of Defense rosters as of September 30, 1990, but did not go to the Persian Gulf War theater before July 31, 1991. This group included approximately half of all such personnel. The number of subjects selected from each service branch was proportional to the number sent to the Gulf War. The date of September 30, 1990, was selected from the Defense Manpower Data Center's quarterly files showing overall military strength because it was the first such file compiled after the start of the war.

The Defense Manpower Data Center provided personal identifiers for the Gulf War veterans and the other veterans in addition to data on their sex, age, race or ethnic group, marital status, branch of service, occupation, rank, pay grade, and total number of months of active military service. The sample was divided into quartiles according to age. Rank was categorized in three levels: enlisted, warrant officer, and officer. Pay grade and length of service were used to determine each veteran's base salary (unadjusted for bonuses and housing allowances), which was categorized in five levels. Occupation (classified by 226 codes) was categorized in 10 major groups as defined in the Occupational Conversion Manual of the Department of Defense.²⁹

Periods of Study

Four periods were selected for study: October 1, 1988, through July 31, 1990 (the "period before the war"); August 1, 1991, to December 31, 1991 ("1991"); January 1 to December 31, 1992 ("1992"); and January 1 to September 30, 1993 ("1993"). The "period before the war" began with the first available triservice (Army, Navy, and Air Force) hospitalization data. Hospitalizations during the Gulf War period itself (from August 1990 through July 1991) were not specifically evaluated, because access to care for Gulf War veterans differed markedly from that for other veterans. In addition, most illnesses said to be related to the Gulf War were reported after July 1991. Because of the high rate of attrition from military service (43.6 percent by October 1993) and the subsequent loss of follow-up, hospitalizations occurring after September 30, 1993, were not studied.

Size of the Study Group

Among the 1,279,931 subjects initially identified, we studied only those for whom data were complete and who were on active duty on the first day of each postwar period. The resulting subgroups contained 1,165,411 subjects for 1991; 1,075,430 for 1992; and 839,389 for 1993.

Hospitalization Data

The hospitalization records included up to eight discharge diagnoses, which were coded by members of the hospital staff using the *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM),³⁰ which groups these codes into 17 broad categories. These data were abstracted by using the Social Security numbers of the study subjects. The risks of any hospitalization and of hospitalization for a diagnosis in each of 14 broad ICD-9-CM categories (not including diagnoses involving the reproductive system) are examined in this report. In each period, a subject was counted only once with regard to each diagnostic category (or hospitalization for any cause), regardless of how often

he or she was hospitalized for conditions in that category. Although the diagnostic fields were scanned in numerical order for the ICD-9-CM codes of interest, no consideration was given to ascertaining the primary cause of hospitalization.

Data Management and Statistical Analysis

Potential demographic risk factors for hospitalization were evaluated by univariate and multivariate tests,³¹ with SAS software (version 6.09, SAS Institute, Cary, N.C.). Hospitalization rates were calculated per 10,000 person-years for the four periods studied and were standardized by the direct method, on the basis of the age and sex distribution of the combined groups of Gulf War veterans and other veterans. Ninety-five percent confidence intervals for the rate ratios were calculated with the method described by Rothman.³²

A multivariate analysis of risk factors was conducted with unconditional, multivariate logistic regression with coefficients estimated by the maximum-likelihood method. To reduce the potential bias due to attrition, only members of the study populations who remained on active duty for at least half the period studied were included in the multivariate models.

RESULTS

Demographic Variables

Information on the demographic characteristics of the study subjects has been placed on file with the National Auxiliary Publications Service (NAPS).^{*} As compared with the other veterans serving in the same era, the Gulf War veterans were disproportionately male (94 percent vs. 88 percent); they were also younger than the other veterans (median age, 25 vs. 27 years). The two groups also differed, but to a lesser extent, with respect to race or ethnic group, marital status, branch of service, rank, salary, and occupation. Accordingly, the hospitalization rates and rate ratios were adjusted for age and sex, and the multiple logistic-regression models were adjusted for all observed demographic differences between the groups.

Potential Bias

We studied the data from the two groups on postwar attrition from active duty and disqualification from service for medical reasons, to identify potential sources of bias. Although the overall age- and sex-adjusted postwar attrition of Gulf War veterans was higher than that of other veterans, the difference was not due to disqualification for medical reasons or mortality (Table 1).

Univariate Analysis

Univariate analyses were performed of hospitalization for any cause and the 14 ICD-9-CM categories of hospitalization for each of the three postwar periods (a total of 45 comparisons). Almost every

^{*}See NAPS document no. 05342 for 3 pages of supplementary material. Order from NAPS c/o Microfiche Publications, P.O. Box 3513, Grand Central Station, New York, NY 10163-3513. Remit in advance (in U.S. funds only) \$7.75 for photocopies or \$5 for microfiche. Outside the U.S. and Canada, add postage of \$4.50 (\$1.75 for microfiche postage). There is a \$15 invoicing charge for all orders filled before payment.

demographic risk factor had a potentially important univariate association ($P \leq 0.25$)³¹ with each outcome.

Multivariate Analysis of Hospitalization for Any Cause

An exploratory stepwise logistic-regression analysis (data not shown) confirmed that almost all the covariates were independently associated with each outcome. Hence, each of the following covariates was included in each logistic-regression model: Gulf War service, sex, age group, race or ethnic group, marital status, branch of service, occupation, rank, salary, and length of military service.

Logistic-regression analysis showed that Gulf War veterans were at slightly lower risk of hospitalization for any cause than other veterans two years before the war but that the risk did not differ after the war (data not shown). Since no triservice data were available from the period before October 1988, data from Navy hospitals on hospitalizations in the Navy and Marine Corps (Naval Health Research Center, San Diego, Calif.) were studied as a surrogate measure. Approximately 109,702 of the 482,034 persons in the combined groups of Gulf War veterans and other veterans in the Navy and Marine Corps in 1991 (23 percent) were on active duty in 1980.

To examine more closely the reduced risk of prewar hospitalization for any cause among Gulf War veterans, we recalculated the adjusted odds ratios (i.e., the odds among Gulf War veterans divided by that among other veterans) for three-month periods (from November 1988 through July 1990 and from August 1991 through July 1993) and plotted them over time (Fig. 1). In a similar fashion, we conducted a multivariate analysis of the Navy and Marine Corps populations from 1980 through July 1990 and from August 1991 through July 1993. There was no difference between Gulf War veterans and other veterans in the risk of hospitalization from 1980 through 1988. However, from 1988 through the time just before the start of the war in August 1990, Gulf War veterans were at lower risk of hospitalization. Shortly after the war ended, the differences in this risk disappeared.

To control for the selection bias that resulted from deploying only the healthiest people in the Persian Gulf, we created a covariate representing prewar hospitalization for inclusion in the multivariate models. This covariate was coded as 1 if a subject was hospitalized for any reason during the 12 months before August 1, 1990, and was coded as 0 otherwise. Risk-factor modeling of hospitalization for any cause showed that women, married personnel, older personnel, whites, Army personnel, and health care workers were the groups more likely to be hospitalized, as were enlisted personnel and persons with the lowest salaries.* The increase in risk among women and married personnel was reduced, but not eliminated, when pregnancy-related hospi-

TABLE 1. STANDARDIZED RATE RATIOS AND 95 PERCENT CONFIDENCE INTERVALS (CI) FOR SEPARATION FROM ACTIVE SERVICE AMONG GULF WAR VETERANS AND OTHER VETERANS, ACCORDING TO THE CAUSE OF SEPARATION, AUGUST 1, 1991, THROUGH DECEMBER 31, 1993, AFTER ADJUSTMENT FOR AGE AND SEX.

CAUSE OF SEPARATION	GULF WAR VETERANS (N=547,076)	OTHER VETERANS (N=618,335)	STANDARDIZED RATE RATIO (95% CI)*
no. of separations			
Medical disqualification	12,048	15,842	0.81 (0.79-0.83)
Dependency or hardship	1,956	2,230	0.94 (0.88-0.99)
Death	724	755	1.03 (0.93-1.14)
Entry into officer program	1,578	2,937	0.61 (0.57-0.64)
Retirement	21,936	42,889	0.82 (0.81-0.83)
Behavior or performance failure	26,902	26,086	0.98 (0.96-0.99)
Expiration of term of service	103,426	77,168	1.28 (1.27-1.30)
Other voluntary separation	17,799	15,919	1.17 (1.15-1.20)
Other involuntary separation†	46,194	41,116	1.25 (1.23-1.27)

*Standardized rate ratios were calculated for Gulf War veterans as compared with other veterans. Hospitalization rates were standardized by the direct method on the basis of the age and sex distribution of the combined groups (Gulf War veterans and other veterans) in August 1991. Confidence intervals were calculated by the method described by Rothman.³²

†Involuntary separations were most often due to reductions by the federal government in the size of the military.

talizations were excluded from the analysis (data not shown).

Multivariate Analysis of Hospitalizations According to ICD-9-CM Category

We studied cohort data both before and after adjustment for the prewar selection effect to determine the risk of hospitalization due to diagnoses in the 14 ICD-9-CM categories in each of the three time periods — that is, in a total of 42 comparisons. Adjustment for the prewar selection effect did not change the odds ratios associated with Gulf War service, but all models reported here include the prewar-hospitalization covariate. The odds of hospitalization differed between the two cohorts in 16 of the 42 comparisons of diagnostic categories (Fig. 2), with Gulf War veterans at greater risk in five models: neoplasms (in 1991), diseases of the genitourinary system (in 1991), diseases of the blood and blood-forming organs (in 1992), and mental disorders (in both 1992 and 1993).

Hospitalizations for Specific Diagnoses

The 10 most frequent diagnoses in each of these five models were examined further with rate calcula-

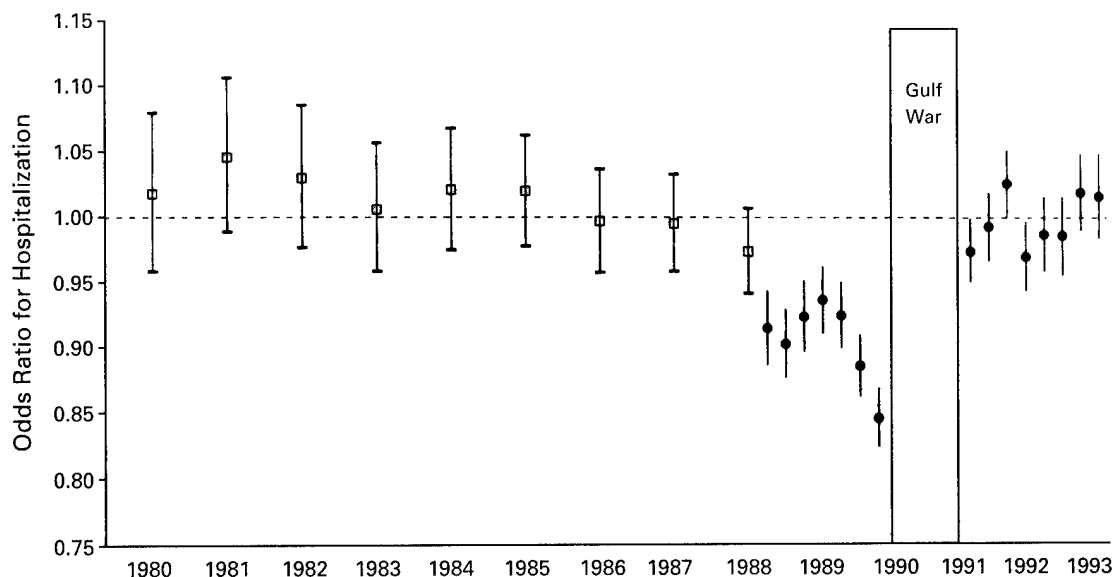


Figure 1. Multivariate Odds Ratios for Hospitalization for Any Cause among Gulf War Veterans as Compared with Other Veterans before and after the War.

Data for the seven successive three-month periods from November 1988 through July 1990 and the eight three-month periods from August 1991 through July 1993 (●) are for Army, Navy, Marine Corps, and Air Force personnel. Calendar-year data from 1980 through 1988 (□) are for Navy and Marine Corps personnel studied similarly, as described in the text. Odds ratios were adjusted for sex, age, race or ethnic group, branch of service, marital status, rank, length of service, salary, and occupation. Vertical lines indicate 95 percent confidence intervals.

tions adjusted for age and sex. These 10 diagnoses accounted for 68 to 100 percent of the diagnoses in their respective categories.

The 10 most frequent discharge diagnoses involving neoplasms in the last five months of 1991 were mostly for benign conditions (Table 2), and most of the 95 percent confidence intervals of the standardized rate ratios showed no significant difference in rates between Gulf War veterans and other veterans. The one exception was the standardized rate ratio and 95 percent confidence interval for testicular cancer, which was slightly elevated over this five-month period. However, this event was rare (29 admissions), and Gulf War veterans were not hospitalized significantly more often with this diagnosis than other veterans in 1992 (standardized rate ratio, 1.39; 95 percent confidence interval, 0.91 to 2.11) or 1993 (standardized rate ratio, 0.89; 95 percent confidence interval, 0.54 to 1.44).

Female Gulf War veterans were at slightly greater risk of hospitalization for disorders of the genitourinary system than other female veterans during the last five months of 1991. Specifically, they were at increased risk for inflammatory diseases of the ovary, fallopian tube, pelvic cellular tissue, and peritoneum (ICD-9-CM code 614) and for infertility (code 628) (Table 2). Male Gulf War veterans were at slightly higher risk of hospitalization than other male veterans for redundant prepuce and phimosis

(code 605), a diagnosis often associated with hospitalization for circumcision. Both male and female Gulf War veterans were at slightly increased risk of being hospitalized for "other disorders of the breast" (code 611), a nonspecific diagnosis. The standardized rate ratios and 95 percent confidence intervals for codes 614, 628, and 611 remained slightly elevated in 1992, but declined in 1993.

Hospitalizations in 1992 for diseases of the blood and blood-forming organs were usually for anemia.* Because of a postwar baby boom among Gulf War veterans, 860 pregnancy-related hospitalizations were removed from consideration, and the multivariate analysis was performed again. The resulting values showed no increase in risk among Gulf War veterans (the 95 percent confidence interval for the odds ratio included 1), suggesting that the increase in risk originally found was primarily due to anemias associated with pregnancy.

Finally, we examined the 10 most frequent diagnoses of mental disorders in 1992 and 1993. Gulf War veterans were hospitalized significantly more often than other veterans for conditions related to al-

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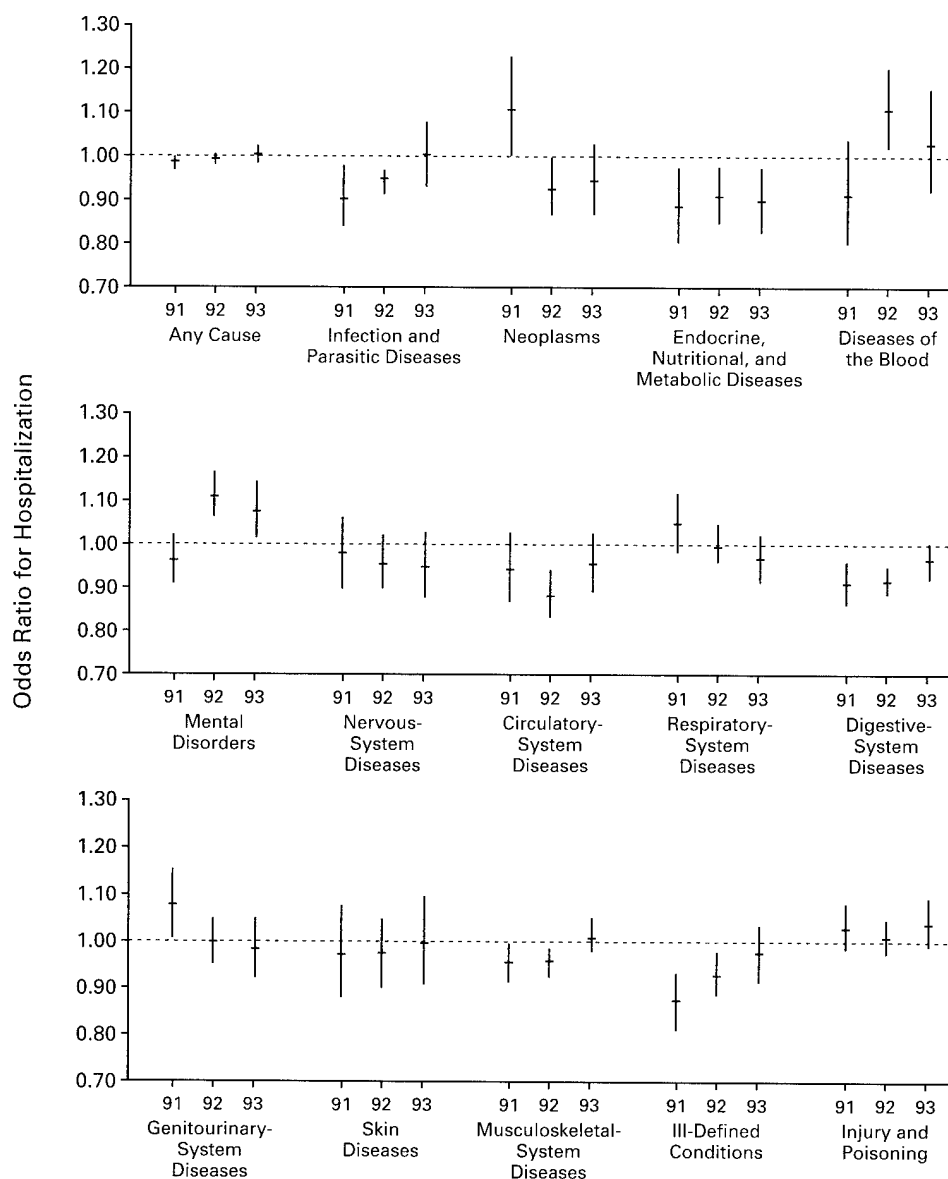


Figure 2. Multivariate Odds Ratios for Hospitalization for Any Cause and for 14 Major ICD-9-CM Diagnostic Categories among Gulf War Veterans as Compared with Other Veterans during the Three Postwar Periods Studied.

Data for 1991, 1992, and 1993 are for the last 5 months of 1991, all 12 months of 1992, and the first 9 months of 1993, respectively. Odds ratios were determined by multivariate logistic-regression analysis, with adjustment for prewar hospitalization, sex, age, race or ethnic group, branch of service, marital status, rank, length of service, salary, and occupation. Vertical lines indicate 95 percent confidence intervals.

cohol and drug use and for adjustment reactions (Table 3).

DISCUSSION

The hospitalization data of the Department of Defense capture the experience of large and demographically well-delineated populations of U.S. adults. These groups are diverse in geographical origin and experience, their socioeconomic status is well known, and because of military requirements, virtually all

their hospitalizations are included in the data base, so that they constitute an excellent resource for epidemiologic studies.³³⁻³⁷ We compared the hospitalization experiences of two large cohorts, totaling 1,165,411 persons in 1991, who remained on active duty after the Persian Gulf War.

These comparisons yielded few surprises. The increased overall risk of hospitalization among women and health care workers* is consistent with the findings of a previous study of hospitalizations in the

TABLE 2. STANDARDIZED RATE RATIOS AND 95 PERCENT CONFIDENCE INTERVALS (CI) FOR HOSPITALIZATION FOR THE 10 MOST FREQUENT DISCHARGE DIAGNOSES IN THE CATEGORIES OF NEOPLASMS AND GENITOURINARY-SYSTEM DISORDERS IN THE STUDY SUBJECTS DURING THE LAST FIVE MONTHS OF 1991, AFTER ADJUSTMENT FOR AGE AND SEX.

ICD-9-CM CODE*	CONDITION	GULF WAR VETERANS	OTHER VETERANS	STANDARDIZED RATE RATIO (95% CI)†
no. of diagnoses				
Neoplasms				
214	Lipoma	192	215	1.12 (0.92–1.36)
218	Uterine leiomyoma‡	59	135	1.22 (0.89–1.65)
211	Benign neoplasm of other parts of digestive system	29	81	0.56 (0.36–0.85)
213	Benign neoplasm of bone and articular cartilage	56	46	1.39 (0.94–2.07)
215	Other benign neoplasm of connective tissue and other soft tissue	34	33	1.37 (0.84–2.24)
216	Benign neoplasm of skin	32	30	1.26 (0.76–2.10)
217	Benign neoplasm of breast	22	38	1.24 (0.73–2.11)
233	Carcinoma in situ of breast and genitourinary system	17	36	1.06 (0.59–1.89)
186	Malignant neoplasm of testis§	29	14	2.12 (1.11–4.02)
239	Neoplasm of unspecified nature	22	19	1.60 (0.85–3.00)
Genitourinary disorders				
614	Inflammatory disease of ovary, fallopian tube, pelvic cellular tissue, and peritoneum	164	285	1.35 (1.11–1.63)
625	Pain and other symptoms associated with female genital organs‡	132	269	1.13 (0.92–1.40)
599	Other disorders of urethra and urinary tract	153	236	0.95 (0.77–1.17)
592	Calculus of kidney and ureter	175	199	1.11 (0.91–1.37)
611	Other disorders of breast	147	164	1.30 (1.03–1.63)
605	Redundant prepuce and phimosis§	144	90	1.59 (1.22–2.07)
608	Other disorders of male genital organs§	94	140	0.74 (0.57–0.97)
622	Noninflammatory disorders of cervix‡	74	134	1.31 (0.98–1.74)
628	Infertility, female‡	78	122	1.59 (1.19–2.11)
617	Endometriosis‡	57	140	1.01 (0.74–1.38)

*ICD-9-CM denotes *International Classification of Diseases, 9th Revision, Clinical Modification*.³⁰

†Standardized rate ratios were calculated for Gulf War veterans as compared with other veterans. Hospitalization rates were standardized by the direct method on the basis of the age and sex distribution of the combined groups (Gulf War veterans and other veterans) in August 1991. Confidence intervals were calculated by the method described by Rothman.³²

‡Only female veterans were considered in this analysis.

§Only male veterans were considered in this analysis.

Navy.³⁸ The increased rates of hospitalization after the war (Table 3) for conditions related to drug and alcohol use and adjustment reactions have been reported in other groups of combat veterans.^{39,40} Finally, the comparisons of separation rates (Table 1) are consistent with the results of other recent mor-

tality studies^{4,5,41} that have not shown Gulf War veterans to have a higher overall or disease-related risk of death than other veterans.

The prewar selection effect we found (Fig. 1) is understandable, in that the services permit recently hospitalized personnel to remain attached to their oper-

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TABLE 3. STANDARDIZED RATE RATIOS AND 95 PERCENT CONFIDENCE INTERVALS (CI) FOR HOSPITALIZATION FOR THE 10 MOST FREQUENT DISCHARGE DIAGNOSES IN THE CATEGORY OF MENTAL DISORDERS IN THE STUDY SUBJECTS DURING 1992 AND THE FIRST NINE MONTHS OF 1993, AFTER ADJUSTMENT FOR AGE AND SEX.

ICD-9-CM CODE*	CONDITION	GULF WAR VETERANS	OTHER VETERANS	STANDARDIZED RATE RATIO (95% CI)†
no. of diagnoses				
Mental disorders in 1992				
303	Alcohol dependence syndrome	2217	2002	1.23 (1.15-1.30)
305	Nondependent abuse of drugs	1258	1244	1.20 (1.11-1.30)
309	Adjustment reaction	1164	1100	1.25 (1.15-1.36)
301	Personality disorders	825	862	1.06 (0.96-1.17)
300	Neurotic disorders	287	462	0.78 (0.67-0.90)
296	Affective psychoses	242	338	0.97 (0.82-1.14)
304	Drug dependence	150	123	1.42 (1.11-1.81)
311	Depressive disorder, not elsewhere classified	117	156	1.03 (0.80-1.31)
307	Special symptoms or syndromes not elsewhere classified	78	121	0.92 (0.69-1.23)
291	Alcoholic psychoses	97	96	1.29 (0.97-1.71)
Mental disorders in 1993				
303	Alcohol dependence syndrome	1143	1129	1.19 (1.10-1.30)
305	Nondependent abuse of drugs	639	707	1.15 (1.03-1.29)
309	Adjustment reaction	517	580	1.09 (0.97-1.24)
301	Personality disorders	331	421	0.90 (0.78-1.04)
300	Neurotic disorders	168	234	0.98 (0.80-1.20)
296	Affective psychoses	143	228	0.88 (0.71-1.09)
304	Drug dependence	66	62	1.30 (0.91-1.85)
311	Depressive disorder, not elsewhere classified	63	98	0.94 (0.68-1.30)
307	Special symptoms or syndromes not elsewhere classified	34	58	0.84 (0.54-1.29)
291	Alcoholic psychoses	37	48	1.03 (0.67-1.59)

*ICD-9-CM denotes *International Classification of Diseases, 9th Revision, Clinical Modification*.³⁰

†Standardized rate ratios were calculated for Gulf War veterans as compared with other veterans. Hospitalization rates were standardized by the direct method on the basis of the age and sex distribution of the combined groups (Gulf War veterans and other veterans) in August 1991. Confidence intervals were calculated by the method described by Rothman.³²

ational units while they convalesce, but the limited-duty status of these personnel makes them ineligible for deployment. The data suggest that this selection effect is transient and that the reduction in the risk of hospitalization seen before the war disappeared shortly after the war (Fig. 1). After we created a prewar-hospitalization covariate to control for this selection effect in the multivariate models, the odds ratios in the two cohorts remained essentially the same.

As would be expected with numerous comparisons, we found some differences in the risks associated with specific diagnostic categories and rates of specific diagnoses. These differences were not consistent over time and do not suggest an emerging illness associated with Gulf War service. Many of the observed differences between cohorts with regard to rates of diagnoses suggest that medical care for some conditions was deferred until after the war. Certain-

ly, this is true with regard to the diagnosis of redundant prepuce and phimosis (ICD-9-CM code 605), which usually means that elective circumcision was performed. Deferred diagnostic evaluation or surgery probably also accounts for the slight increases in the rates of various benign neoplasms (Table 2) and of hospitalizations for inflammatory disease or infertility in women (Table 3) that occurred immediately after the war. Because no known associations between an exposure and the appearance of a neoplasm have such a short latency period and because women are hospitalized for infertility only after months, if not years, of outpatient medical care, it is difficult to implicate Gulf War service in causing these conditions. It is more likely that Gulf War veterans waited until they were home before undergoing elective hospitalization.

These analyses have a number of strengths. The large groups studied, for which there were detailed demographic data to mitigate confounding, offer unusually high statistical power to detect differences in the risk of hospitalization. Because discharge data are recorded thoroughly by hospitals associated with the Department of Defense and because personnel on active duty have little opportunity to be hospitalized outside these hospitals, nearly all the hospitalizations of Gulf War veterans are represented in the data we used. In addition, all veterans are screened medically, with interviews, physical examinations, and laboratory studies, before their separation from military service. Free medical care by the Department of Defense and potentially lifelong medical-disability benefits are strong incentives for veterans to report their maladies thoroughly. Therefore, it is unlikely that any hospitalization occurring before the time of separation from the military would have gone unnoticed.

These analyses also have limitations. Our broad categorization of a person's status as a Gulf War veteran or another type of veteran may mask the detection of illness that has a temporally or geographically specific exposure as the cause. All the logistic-regression models were adjusted for the prewar selection effect, but if this adjustment was inadequate, slight increases in the risk of hospitalization among Gulf War veterans might not be detected. The study data reflect only the hospitalization experience of persons who remained on active duty through September 1993; illnesses associated with exposure during the Gulf War whose latency periods are longer than two years would have been missed. Similarly, illness occurring after a veteran's separation from the military would have been missed. In addition, illnesses not requiring hospitalization are not represented in our data. Finally, the increased attention in the media and awareness by the public concerning morbidity among Gulf War veterans may have influenced rates of postwar hospitalization among such veterans.²³

This bias should have increased the likelihood of such hospitalizations, however.

In conclusion, we constructed multivariate logistic-regression models for hospitalization both overall and for conditions assigned to any of 14 broad diagnostic categories in each of three postwar periods. The risk associated with 16 of these 45 comparisons differed between Gulf War veterans and other veterans. In 5 of these 16 cases, the risk of hospitalization was higher among Gulf War veterans, but the increases were inconsistent over time and were probably due to deferred medical care, a postwar baby boom, chance, or mental conditions known to be associated with war. The data suggest that veterans of the Gulf War who remained on active duty were not at increased risk for unexplained hospitalization during the 25 months after the war.

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REFERENCES

1. Congressional Research Service. Iraq-Kuwait crisis: a chronology of events, July 17, 1990–December 23, 1991. Washington, D.C.: Library of Congress, 1992.
2. Best FM, Tomich N. Medicine in the Gulf War. Washington, D.C.: U.S. Medicine, 1995.
3. Helmkamp JC. Epidemiological characteristics of U.S. fatalities during Desert Storm. *Mil Med* 1992;157:A7.
4. *Idem*. United States military casualty comparison during the Persian Gulf War. *J Occup Med* 1994;36:609-15.
5. Writer JV, DeFraitres RF, Brundage JF. Comparative mortality among US military personnel in the Persian Gulf region and worldwide during Operations Desert Shield and Desert Storm. *JAMA* 1996;275:118-21.
6. Hyams KC, Hanson K, Wignall FS, Escamilla J, Oldfield EC III. The impact of infectious diseases on the health of U.S. troops deployed to the Persian Gulf during operations Desert Shield and Desert Storm. *Clin Infect Dis* 1995;20:1497-504.
7. Persian Gulf Veterans Coordinating Board. Unexplained illnesses among Desert Storm veterans: a search for causes, treatment, and cooperation. *Arch Intern Med* 1995;155:262-8.
8. Cotton P. Gulf War symptoms remain puzzling. *JAMA* 1992;268:2619.
9. Brown D. Diagnosis unknown: Gulf War syndrome. *Washington Post*. July 24, 1994.
10. DeFraitres RF, Wanat ER, Norwood AE, Williams S, Cowan D, Callahan T. Investigation of a suspected outbreak of an unknown disease among

veterans of Operation Desert Shield/Storm, 123rd Army Reserve Command, Fort Benjamin Harrison, Indiana, April 1992. Washington, D.C.: Division of Preventive Medicine, Walter Reed Army Institute of Research, 1992.

11. Committee to Review the Health Consequences of Service during the Persian Gulf War, Medical Follow-up Agency, Institute of Medicine. Health consequences of service during the Persian Gulf War: initial findings and recommendations for immediate action. Washington, D.C.: National Academy Press, 1995.
12. Milner IB, Axelrod BN, Pasquantonio J, Sillanpaa M. Is there a Gulf War syndrome? *JAMA* 1994;271:661.
13. Stretch RH, Bliese PD, Marlowe DH, Wright KM, Knudson KH, Hoover CH. Physical health symptomatology of Gulf War-era service personnel from the states of Pennsylvania and Hawaii. *Mil Med* 1995;160:131-6.
14. Unexplained illness among Persian Gulf veterans in an Air National Guard unit: preliminary report — August 1990–March 1995. *MMWR Morb Mortal Wkly Rep* 1995;44:443-7.
15. Comprehensive Clinical Evaluation Program for Gulf War veterans: report on 18,598 participants. Washington, D.C.: Department of Defense, 1996.
16. Kang HK, Dalager NA, Lee KY. Health surveillance of Persian Gulf War veterans: a review of the Department of Veterans Affairs Persian Gulf Registry and in-patient treatment files. Washington, D.C.: Environmental Epidemiology Service, Department of Veterans Affairs, 1995.
17. Defense Science Board. Report of the Defense Science Board Task Force on Persian Gulf War health effects. Washington, D.C.: Office of the Undersecretary of Defense for Acquisition and Technology, 1994.
18. National Institutes of Health Technology Assessment Workshop Panel. The Persian Gulf experience and health. *JAMA* 1994;272:391-6.
19. Cowley G, Hager M, Liu M. Tracking the second storm. *Newsweek*. May 16, 1994:56-7.
20. Tippet S. What's wrong with our children? *Ladies Home Journal*. June 1994;100, 148.
21. France D. The families who are dying for our country. *Redbook*. September 1994;114, 148.
22. Flanders L. A lingering sickness. *The Nation*. January 23, 1995:94-6.
23. Fumento M. What Gulf War syndrome? *American Spectator*. May 1995:28-34.
24. Nelson S. Hotline for sick vets. *Navy Times*. July 4, 1995:10.
25. DoD opens additional Persian Gulf hotline. *Persian Gulf Review*. August 1995:5.
26. Jehl D. Clinton to create a panel to look into Gulf War illnesses. *New York Times*. March 7, 1995:A14.
27. Nelson S. Gulf ills spur new studies. *Army Times*. June 19, 1995.
28. Executive order 12744: designation of Arabian Peninsula areas, air-space and adjacent waters as a combat zone. *Fed Regist* 1991;56(15):2663.
29. Occupational conversion manual: enlisted/officer/civilian. Washington, D.C.: Office of the Assistant Secretary of Defense, 1991.
30. Department of Health and Human Services. The international classification of diseases, 9th rev., clinical modification: ICD-9-CM, 3rd ed. Vol. 1. Washington, D.C.: Government Printing Office, 1989. (DHHS publication no. (PHS) 89-1260.)
31. Model-building strategies and methods for logistic regression. In: Hosmer DW Jr, Lemeshow S. *Applied logistic regression*. New York: John Wiley, 1989:82-134.
32. Rothman KJ. *Modern epidemiology*. Boston: Little, Brown, 1986:144, 231.
33. Comstock GW, Edwards LB, Livesay VT. Tuberculosis morbidity in the US Navy: its distribution and decline. *Am Rev Respir Dis* 1974;110:572-80.
34. Arday DR, Kanjarpane DD, Kelley PW. Mumps in the US Army 1980-86: should recruits be immunized? *Am J Public Health* 1989;79:471-4.
35. Garland FC, Shaw EK, Gorham ED, Garland CF, White MR, Sinsheimer PJ. Incidence of leukemia in occupations with potential electromagnetic field exposure in United States Navy personnel. *Am J Epidemiol* 1990;132:293-303.
36. Gray GC, Palinkas LA, Kelley PW. Increasing incidence of varicella hospitalizations in United States Army and Navy personnel: are today's teenagers more susceptible? Should recruits be vaccinated? *Pediatrics* 1990;86:867-73.
37. Gray GC, Mitchell BS, Tueller JE, Cross ER, Amundson DE. Pneumonia hospitalizations in the US Navy and Marine Corps: rates and risk factors for 6,522 admissions, 1981-1991. *Am J Epidemiol* 1994;139:793-802.
38. Hoiberg A. Sex and occupational differences in hospitalization rates among Navy enlisted personnel. *J Occup Med* 1980;22:685-90.
39. Hobfoll SE, Spielberger CD, Breznitz S, et al. War-related stress: addressing the stress of war and other traumatic events. *Am Psychol* 1991;46:848-55.
40. Sutker PB, Uddo M, Brailey K, Allain AN, Errera P. Psychological symptoms and psychiatric diagnoses in Operation Desert Storm troops serving Graves registration duty. *J Traumatic Stress* 1994;7:159-71.
41. Kang HK, Bullman TA. Mortality among U.S. veterans of the Persian Gulf War. *N Engl J Med* 1996;335:1498-504.

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